

WHAT IS CLAIMED IS:

1 1. A composition for the treatment of an anorectal disorder, and for
2 controlling the pain associated therewith, said composition comprising a NO donor in
3 admixture with a second agent selected from the group consisting of phosphodiesterase
4 type II inhibitors, phosphodiesterase type IV inhibitors, phosphodiesterase type V
5 inhibitors, nonspecific phosphodiesterase inhibitors, superoxide scavengers, β -adrenergic
6 agonists, cAMP-dependent protein kinase activators, α_1 -adrenergic antagonists, estrogens,
7 ATP-sensitive K^+ channel activators and smooth muscle relaxants, with a
8 pharmaceutically acceptable carrier.

1 2. A composition in accordance with claim 1, wherein said NO donor
2 is selected from the group consisting of nitroglycerin, L-arginine, SNAP, GSNO and SIN-
3 1, and said second agent is a superoxide scavenger selected from the group consisting of
4 superoxide dismutase and chemical superoxide dismutase mimetics.

1 3. A composition in accordance with claim 1, wherein said carrier is
2 formulated for local application.

1 4. A composition in accordance with claim 1, wherein said second
2 agent is selected from the group consisting of phosphodiesterase type II inhibitors,
3 phosphodiesterase type IV inhibitors, phosphodiesterase type V inhibitors, and
4 nonspecific phosphodiesterase inhibitors.

1 5. A composition in accordance with claim 1, wherein said second
2 agent is selected from the group consisting of β -adrenergic agonists.

1 6. A composition in accordance with claim 5, wherein said β -
2 adrenergic agonist is selected from the group consisting of β_2 -adrenergic agonists and
3 β_3 -adrenergic agonists.

1 7. A composition in accordance with claim 1, wherein said second
2 agent is selected from the group consisting of ATP-sensitive K^+ channel activators.

1 8. A composition for the treatment of an anorectal disorder, and for
2 controlling the pain associated therewith, said composition comprising a
3 phosphodiesterase inhibitor and a pharmaceutically acceptable carrier.

1 9. A composition in accordance with claim 8, wherein said
2 phosphodiesterase inhibitor is selected from the group consisting of phosphodiesterase
3 type II inhibitors, phosphodiesterase type IV inhibitors, phosphodiesterase type V
4 inhibitors, and nonspecific phosphodiesterase inhibitors.

1 10. A composition in accordance with claim 9, further comprising an
2 agent selected from the group consisting of β -adrenergic agonists, cAMP-dependent
3 protein kinase activators, α_1 -adrenergic antagonists, L-type Ca^{2+} channel blockers,
4 estrogens, ATP-sensitive K^+ channel activators and smooth muscle relaxants.

1 11. A composition for the treatment of an anorectal disorder, and for
2 controlling the pain associated therewith, said composition comprising a β -adrenergic
3 agonist and a pharmaceutically acceptable carrier.

1 12. A composition in accordance with claim 11, wherein said β -
2 adrenergic agonist is specific for a receptor isoform selected from the group consisting of
3 β_2 , β_3 and combinations thereof.

1 13. A composition in accordance with claim 11, wherein said β -
2 adrenergic agonist is isoproterenol.

1 14. A composition in accordance with claim 11, further comprising an
2 agent selected from the group consisting of cAMP-hydrolyzing PDE inhibitors,
3 nonspecific PDE inhibitors, α_1 -adrenergic antagonists, estrogens, L-type Ca^{2+} channel
4 blockers, ATP-sensitive K^+ channel activators and smooth muscle relaxants.

1 15. A composition for the treatment of an anorectal disorder, and for
2 controlling the pain associated therewith, said composition comprising an ATP-sensitive
3 K^+ channel activator and a pharmaceutically acceptable carrier.

1 16. A composition in accordance with claim 15, further comprising an
2 agent selected from the group consisting of cAMP-dependent protein kinase activators,
3 estrogens, α_1 -adrenergic antagonists, L-type Ca^{2+} channel blockers and smooth muscle
4 relaxants.

1 17. A composition for the treatment of an anorectal disorder, and for
2 controlling the pain associated therewith, said composition comprising an α_1 -adrenergic
3 antagonist and a pharmaceutically acceptable carrier.

1 18. A composition in accordance with claim 17, said composition
2 further comprising an agent selected from the group consisting of cAMP-hydrolyzing
3 phosphodiesterase inhibitors, estrogens and smooth muscle relaxants.

1 19. A composition in accordance with claim 17, wherein said cAMP-
2 hydrolyzing phosphodiesterase inhibitor is a phosphodiesterase type IV inhibitor.

1 20. A composition for the treatment of an anorectal disorder, and for
2 controlling the pain associated therewith said composition comprising a cAMP-dependent
3 protein kinase activator and an L-type Ca^{2+} channel blocker.

1 21. A composition for the treatment of an anorectal disorder, and for
2 controlling the pain associated therewith, said composition comprising a cGMP-
3 dependent protein kinase activator and a pharmaceutically acceptable carrier..

1 22. A composition for the treatment of an anorectal disorder, and for
2 controlling the pain associated therewith, said composition comprising a nonspecific
3 cyclic nucleotide-dependent protein kinase activator, optionally in admixture with a
4 smooth muscle relaxant.

1 23. A method of treating an anorectal disorder, and for controlling the
2 pain associated therewith, the method comprising administering to a subject in need of
3 such treatment a therapeutically effective amounts of a NO donor and a second agent
4 selected from the group consisting of phosphodiesterase type II inhibitors,
5 phosphodiesterase type IV inhibitors, phosphodiesterase type V inhibitors, nonspecific
6 phosphodiesterase inhibitors, superoxide scavengers, β -adrenergic agonists, cAMP-
7 dependent protein kinase activators, α_1 -adrenergic antagonists, estrogens, L-type Ca^{2+}
8 channel blockers, ATP-sensitive K^+ channel activators and smooth muscle relaxants.

1 24. A method in accordance with claim 23, wherein said NO donor and
2 said second agent are administered in combination.

1 25. A method in accordance with claim 23, wherein said second agent
2 is administered prior to said NO donor.

1 26. A method in accordance with claim 23, wherein said anorectal
2 disorder is an anal fissure.

1 27. A method of treating an anorectal disorder, and for controlling the
2 pain associated therewith, the method comprising administering to a subject in need of
3 such treatment a therapeutically effective amount of a composition comprising a
4 phosphodiesterase inhibitor.

1 28. A method in accordance with claim 27, further comprising
2 administering to said subject a second agent selected from the group consisting of β -
3 adrenergic agonists, cAMP-dependent protein kinase activators, α_1 -adrenergic
4 antagonists, estrogens, L-type Ca^{2+} channel blockers, ATP-sensitive K^+ channel activators
5 and smooth muscle relaxants.

1 29. A method of treating an anorectal disorder, and for controlling the
2 pain associated therewith, the method comprising administering to a subject in need of
3 such treatment a therapeutically effective amount of a composition comprising a β -
4 adrenergic agonist.

1 30. A method in accordance with claim 29, further comprising
2 administering to said subject a second agent selected from the group consisting of cAMP-
3 dependent protein kinase activators, α_1 -adrenergic antagonists, estrogens, L-type Ca^{2+}
4 channel blockers, ATP-sensitive K^+ channel activators and smooth muscle relaxants.

1 31. A method of treating an anorectal disorder, and for controlling the
2 pain associated therewith, the method comprising administering to a subject in need of
3 such treatment a therapeutically effective amount of a composition comprising an ATP-
4 sensitive potassium channel opener and an agent that promotes cAMP-mediated anal
5 sphincter relaxation.

1 32. A method of treating an anorectal disorder, and for controlling the
2 pain associated therewith, the method comprising administering to a subject in need of
3 such treatment a therapeutically effective amount of a composition comprising a

4 . potassium channel opener, wherein said therapeutically effective amount decreases
5 hypertonicity of an anal sphincter muscle of the subject.

1 33. A method of treating an anorectal disorder, and for controlling the
2 pain associated therewith, the method comprising administering to a subject in need of
3 such treatment a therapeutically effective amount of a composition comprising a
4 pharmaceutically acceptable carrier and an agent which increases a level of cyclic
5 guanidine monophosphate or cyclic adenosine monophosphate in a tissue of an anal
6 sphincter muscle of the subject, thereby decreasing hypertonicity of the anal sphincter
7 muscle of the subject.

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